



## **BAYER UPDATES LABELS FOR YAZ and YASMIN**

### ***Body of Evidence Affirms VTE Risk/Benefit Profile for YAZ and Yasmin Is Comparable to Other Combination Oral Contraceptives***

**Wayne, NJ, April 9, 2010** – In full agreement with the U.S. Food and Drug Administration (FDA), Bayer HealthCare Pharmaceuticals, Inc. today announced that it will update the labels for YAZ<sup>®</sup> (3 mg drospirenone / 0.02 mg ethinyl estradiol) and Yasmin<sup>®</sup> (3 mg drospirenone / 0.03 mg ethinyl estradiol) in the United States. The updated labels confirm that the body of evidence continues to support that the relative risk of developing venous thromboembolism (VTE) in YAZ and Yasmin users is comparable to that of other combination oral contraceptive preparations, including those containing levonorgestrel. The labels also state, unchanged, that there is a risk of VTE among all combination oral contraceptives (a class effect), and provides additional information and context about data specific to drospirenone containing oral contraceptives.

“The FDA’s thoughtful and balanced analysis will provide helpful information for healthcare professionals to use when they are providing guidance and counsel to patients,” said Kemal Malik, MD, Chief Medical Officer at Bayer HealthCare. “In weighing the evidence on the relative risk of combination oral contraceptives, the FDA has underscored the importance of protocol methodology on the outcomes and findings of scientific studies and we appreciate the rigor they have applied to their analysis.”

Several studies have investigated the relative risks of thromboembolism in women using drospirenone containing combination oral contraceptives (COCs) compared to women using COCs containing other progestins. At the time of Yasmin approval in 2001, Bayer commissioned two independently conducted large prospective observational studies of more than 120,000 COC users in the U.S. and Europe. Among the outcomes studied, a predefined endpoint of these studies evaluated the risk of venous and arterial thromboembolism and death in oral contraceptive users. Reflecting this body of evidence, the new labels now state:

- A prospective cohort study (EURAS<sup>1</sup>), conducted in Europe, showed the risk of thromboembolism (particularly venous thromboembolism) and death in Yasmin users to be comparable to that of oral contraceptive preparations, including those containing levonorgestrel.

- Another prospective cohort study (Ingenix<sup>2</sup>), conducted in the USA, also showed a comparable risk of thromboembolism in Yasmin users compared to users of other COCs, including those containing levonorgestrel. In this study, COC comparator groups were selected based on having similar characteristics to those being prescribed Yasmin.

As part of its evaluation of the risk/benefit of YAZ and Yasmin, the FDA also reviewed data from one case-control study (van Hylckama Vlieg *et al.*<sup>3</sup>) and one retrospective study (Lidegaard *et al.*<sup>4</sup>) which suggested that the risk of venous thromboembolism occurring in Yasmin users was between the risk associated with levonorgestrel-containing COCs and desogestrel/gestodene-containing COCs.

Based on the FDA's review, the new labels now state that key conclusions from both studies are unreliable:

- With regard to the case-control study, the label indicates that, "...the number of Yasmin cases was very small (1.2% of all cases) making the risk estimates unreliable."
- Concerning the retrospective cohort study, the label indicates that, "The relative risk for Yasmin users in the retrospective cohort study was greater than that for users of other COCs when considering women who used the products for less than one year. However, these one-year estimates may not be reliable because the analysis may include women of varying risk levels. Among women who used the product for one to four years, the relative risk was similar for users of Yasmin to that for users of other COCs."

Bayer continues its commitment to study the safety and efficacy of oral contraceptives, including YAZ and Yasmin, and is supporting another independently conducted study in the US and Europe (INAS). The data from the INAS study are expected in 2011.

"At Bayer, our unwavering commitment to our customers' health and well-being is always our first priority and we will continue to provide information which will support health care providers and their patients in making informed decisions about appropriate treatment choices," said Dr. Malik. "These data confirm that the benefit/risk profiles for YAZ and Yasmin remain unchanged. We are convinced that YAZ and Yasmin are good choices for women seeking safe and effective contraception if they use the products as directed."

#### **About Bayer HealthCare Pharmaceuticals Inc.**

Bayer HealthCare Pharmaceuticals Inc. is the U.S.-based pharmaceuticals operation of Bayer HealthCare LLC, a division of Bayer AG. One of the world's leading, innovative companies in the healthcare and medical products industry, Bayer HealthCare combines the global activities of the Animal Health, Consumer Care, Diabetes Care, and Pharmaceuticals divisions. In the United States,

Bayer HealthCare Pharmaceuticals comprises the following business units: Women's Healthcare, Diagnostic Imaging, General Medicine, Hematology/Neurology, and Oncology. The company's aim is to discover and manufacture products that will improve human health worldwide by diagnosing, preventing and treating diseases.

### **Important Safety Information about YAZ and Yasmin**

**YASMIN**<sup>®</sup> (drospirenone & ethinyl estradiol) is indicated for the prevention of pregnancy in women who elect to use an oral contraceptive. **YAZ**<sup>®</sup> (drospirenone & ethinyl estradiol) is indicated for:

- The prevention of pregnancy in women who elect to use an oral contraceptive.
- Treatment of the emotional and physical symptoms of premenstrual dysphoric disorder (PMDD) in women who choose to use an oral contraceptive as their method of contraception.
  - The effectiveness of YAZ for PMDD when used for more than 3 menstrual cycles has not been evaluated. YAZ has not been evaluated for the treatment of premenstrual syndrome (PMS).
- Treatment of moderate acne vulgaris
  - In women at least 14 years of age, who have no known contraindications to oral contraceptive therapy and have achieved menarche. YAZ should be used for the treatment of moderate acne only if the patient desires an oral contraceptive for birth control.

**Who Shouldn't Take Any Oral Contraceptives (OCs)?** Some women should not use OCs, including women who have blood clots, certain cancers, a history of heart attack or stroke, as well as those who are or may be pregnant.

**In Addition, Who Shouldn't Take YAZ or Yasmin?** YAZ and Yasmin each contains a different kind of hormone (drsp<sup>®</sup>) that for some may increase potassium too much. Therefore, you should not take YAZ or Yasmin if you have kidney, liver, or adrenal disease because this could cause serious heart and health problems. Tell your healthcare provider if you are on daily long-term treatment for a chronic condition such as cardiovascular disease or chronic inflammatory disease. Women who take certain drugs (see below) should have their potassium levels checked in the first month of taking YAZ or Yasmin.

**What Drugs May Increase Potassium?** NSAIDs-ibuprofen (Motrin<sup>®</sup>, Advil<sup>®</sup>), naproxen (Naprosyn<sup>®</sup>, Aleve<sup>®</sup>, and others) when taken long-term and daily for arthritis or other diseases or conditions, Potassium-sparing diuretics (spironolactone and others), Potassium supplementation, ACE inhibitors (Capoten<sup>®</sup>, Vasotec<sup>®</sup>, Zestril<sup>®</sup>, and others), angiotensin-II receptor antagonists (Cozaar<sup>®</sup>, Diovan<sup>®</sup>, Avapro<sup>®</sup>, and others), aldosterone antagonists, and heparin.

**What Are The Risks Involved With Taking Any Oral Contraceptive (OC)?** OCs can be associated with an increased risk of several serious cardiovascular side effects, including blood clots, stroke, and heart attack. **Women, especially those 35 and over, are strongly advised not to smoke because it increases these risks. OCs do not protect against HIV infection or other STDs.**

**The most frequent (greater than 1%) side effects, which may or may not be related to YAZ, that were present in all YAZ clinical trials included:** upper respiratory infection, headache, breast pain,

vaginal moniliasis, nausea, abdominal pain, dysmenorrhea, urinary tract infection, accidental injury, sinusitis, emotional lability, suspicious Papanicolaou smear, weight gain, depression, menstrual disorder, and asthenia.

**The most frequent (greater than 1%) side effects, which may or may not be related to YAZ, that were either unique to each trial type or occurred in only two types of clinical trials included:**

- **In the contraception trial:** leukorrhea, diarrhea, vomiting, vaginitis, flu syndrome, moniliasis, allergic reaction, cystitis, tooth disorder, sore throat, infection, fever, surgery, back pain, migraine, dyspepsia, rhinitis, acne, gastroenteritis, bronchitis, pharyngitis, skin disorder, intermenstrual bleeding, decreased libido, pain, increased cough, dizziness, pain in extremity, and pelvic pain.
- **In the PMDD trials:** intermenstrual bleeding, decreased libido, nervousness, menorrhagia, pain in extremity, migraine, vaginitis, hyperlipidemia, back pain, diarrhea, increased appetite, enlarged abdomen, and acne.
- **In the acne trials:** metrorrhagia, flu syndrome, menorrhagia, gastroenteritis, tooth disorder, infection, vomiting, pharyngitis, sore throat, arthralgia, bronchitis, rhinitis, amenorrhea, and urine abnormality.

**You are encouraged to report negative side effects of prescription drugs to the FDA. Visit [www.fda.gov/medwatch](http://www.fda.gov/medwatch), or call 1-800-FDA-1088.**

**For important safety information**, including boxed warnings about YAZ and Yasmin, please see the full prescribing information at [bayerbirthcontrol.com](http://bayerbirthcontrol.com).

Women who would like to learn more about YAZ should call the toll-free number 1-888-84-BAYER or visit [www.yaz-us.com](http://www.yaz-us.com).

BAYER®, the Bayer Cross®, YAZ®, Aleve®, drsp® and Beyond Birth Control are trademarks of Bayer. All other trademarks are the property of their respective owners.

# # #

<sup>1</sup> Dinger, Jürgen et al.: The safety of a drospirenone-containing oral contraceptive: final results from the European Active Surveillance study on Oral Contraceptives based on 142,475 women-years of observation. In: Contraception, 75, 2007, 344– 354.

<sup>2</sup> Seeger, John et al.: Risk of Thromboembolism in Women Taking Ethinylestradiol/Drospirenone and Other Oral Contraceptives. In: Obstetrics & Gynecology, Vol. 110, No. 3, September 2007, 587 – 893.

<sup>3</sup> Van Hylckama Vlieg A, Helmerhorst FM, Vandenbroucke JP, Doggen CJ, Rosendaal FR. The venous thrombotic risk of oral contraceptives, effects of oestrogen dose and progestogen type: results of the MEGA case-control study. BMJ. 2009;339:b2921.

<sup>4</sup> Lidegaard O, Lokkegaard E, Svendsen AL, Agger C. Hormonal contraception and risk of venous thromboembolism: national follow-up study. BMJ. 2009;339:b2890.

## **Contacts**

**Media:** Rose Talarico, Bayer HealthCare, [rose.talarico@bayer.com](mailto:rose.talarico@bayer.com), (973) 305-5302

*This news release may contain forward-looking statements based on current assumptions and forecasts made by Bayer Group or subgroup management. Various known and unknown risks, uncertainties and other factors could lead to material differences between the actual future results, financial situation, development or performance of the company and the estimates given here. These factors include those discussed in Bayer's public reports which are available on the Bayer website at [www.bayer.com](http://www.bayer.com). The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.*